

SEQUENCE LISTING

<110> SOLVAY PHARMACEUTICALS GmbH

<120> Compounds With NEP/MP-Inhibitory Activity
and Uses Thereof

<130> HA 00.17-WO

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<170> PatentIn Ver. 2.1

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Ala Ala Ala Arg Ile Leu Gln Asn Met Asp Pro Thr Thr Glu Pro Cys	
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Phe	Phe	Ser	Lys	Glu	Gln	Pro	Gln	Ala	Leu	Asn	Phe	Gly	Gly	Ile																																																				

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Thr Gln His Phe Arg Glu Gln Ser Glu Cys Met Ile Tyr Gln Tyr Gly	
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aac tac tcc tgg gac ctg gca gac gaa cag aac gtg aac gga ttc aac	2016
Asn Tyr Ser Trp Asp Leu Ala Asp Glu Gln Asn Val Asn Gly Phe Asn	
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Lys Ala Tyr Leu Lys Trp Met Ala Glu Gly Gly Lys Asp Gln Gln Leu	
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Pro Gly Leu Asp Leu Thr His Glu Gln Leu Phe Phe Ile Asn Tyr Ala	
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Gln Val Trp Cys Gly Ser Tyr Arg Pro Glu Phe Ala Ile Gln Ser Ile	
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Lys Thr Asp Val His Ser Pro Leu Lys Tyr Arg Val Leu Gly Ser Leu	
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Gln Asn Leu Ala Ala Phe Ala Asp Thr Phe His Cys Ala Arg Gly Thr	
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 35 40 45
 Asp Arg Arg Gly Lys Gln Leu Pro Arg Leu Ala Ser Arg Leu Cys Phe
 50 55 60
 Leu Gln Glu Glu Arg Thr Phe Val Lys Arg Lys Pro Arg Gly Ile Pro

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Glu	Leu	Glu	Val	Ile	Leu	Lys	Ala	Val	Leu	Glu	Asn	Ser	Thr	Ala	Lys
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Asp	Arg	Pro	Ala	Val	Glu	Lys	Ala	Arg	Thr	Leu	Tyr	Arg	Ser	Cys	Met
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Leu	Glu	Val	Val	Gly	Gly	Trp	Pro	Val	Ala	Met	Asp	Arg	Trp	Asn	Glu
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Thr	Val	Gly	Leu	Glu	Trp	Glu	Leu	Glu	Arg	Gln	Leu	Ala	Leu	Met	Asn
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Val	Arg	Glu	Ala	Tyr	Leu	Gln	Phe	Met	Val	Ser	Val	Ala	Thr	Leu	Leu
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Arg	Glu	Asp	Ala	Asn	Leu	Pro	Arg	Asp	Ser	Cys	Leu	Val	Gln	Glu	Asp
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Asn 385	Ile	Ile	Asp	Thr	Tyr 390	Ser	Ala	Arg	Thr	Ile 395	Gln	Asn	Tyr	Leu	Val 400
Trp	Arg	Leu	Val	Leu 405	Asp	Arg	Ile	Gly	Ser 410	Leu	Ser	Gln	Arg	Phe	Lys 415
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Glu	Val	Arg 435	Trp	Arg	Glu	Cys	Val 440	Gly	Tyr	Val	Asn	Ser 445	Asn	Met	Glu
Asn	Ala 450	Val	Gly	Ser	Leu	Tyr 455	Val	Arg	Glu	Ala	Phe 460	Pro	Gly	Asp	Ser
Lys 465	Ser	Met	Val	Arg 470	Glu	Leu	Ile	Asp	Lys	Val 475	Arg	Thr	Val	Phe	Val 480
Glu	Thr	Leu	Asp 485	Glu	Leu	Gly	Trp	Met	Asp 490	Glu	Glu	Ser	Lys	Lys 495	Lys
Ala	Gln	Glu	Lys 500	Ala	Met	Ser	Ile	Arg 505	Glu	Gln	Ile	Gly	His 510	Pro	Asp
Tyr	Ile 515	Leu	Glu	Glu	Met	Asn	Arg 520	Arg	Leu	Asp	Glu	Glu 525	Tyr	Ser	Asn
Leu 530	Asn	Phe	Ser	Glu	Asp	Leu 535	Tyr	Phe	Glu	Asn	Ser 540	Leu	Gln	Asn	Leu
Lys 545	Val	Gly	Ala	Gln	Arg 550	Ser	Leu	Arg	Lys	Leu 555	Arg	Glu	Lys	Val	Asp 560
Pro	Asn	Leu	Trp 565	Ile	Ile	Gly	Ala	Ala 570	Val	Val	Asn	Ala	Phe 575	Tyr	Ser
Pro	Asn	Arg 580	Asn	Gln	Ile	Val	Phe	Pro 585	Ala	Gly	Ile	Leu	Gln 590	Pro	Pro
Phe	Phe 595	Ser	Lys	Glu	Gln	Pro	Gln 600	Ala	Leu	Asn	Phe 605	Gly	Gly	Ile	Gly
Met 610	Val	Ile	Gly	His	Glu	Ile 615	Thr	His	Gly	Phe 620	Asp	Asp	Asn	Gly	Arg
Asn 625	Phe	Asp	Lys	Asn	Gly 630	Asn	Met	Met	Asp	Trp 635	Trp	Ser	Asn	Phe	Ser 640
Thr	Gln	His	Phe 645	Arg	Glu	Gln	Ser	Glu	Cys 650	Met	Ile	Tyr	Gln	Tyr 655	Gly
Asn	Tyr	Ser 660	Trp	Asp	Leu	Ala	Asp	Glu 665	Gln	Asn	Val	Asn	Gly 670	Phe	Asn
Thr	Leu	Gly	Glu	Asn	Ile	Ala	Asp	Asn	Gly	Gly	Val	Arg	Gln	Ala	Tyr

675					680					685					
Lys	Ala	Tyr	Leu	Lys	Trp	Met	Ala	Glu	Gly	Gly	Lys	Asp	Gln	Gln	Leu
690					695					700					
Pro	Gly	Leu	Asp	Leu	Thr	His	Glu	Gln	Leu	Phe	Phe	Ile	Asn	Tyr	Ala
705					710					715					720
Gln	Val	Trp	Cys	Gly	Ser	Tyr	Arg	Pro	Glu	Phe	Ala	Ile	Gln	Ser	Ile
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Lys	Thr	Asp	Val	His	Ser	Pro	Leu	Lys	Tyr	Arg	Val	Leu	Gly	Ser	Leu
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Ala Gly Gln Lys Arg Pro Gly Phe Leu Glu Gly Gly Leu Leu Leu Leu																
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ctg ctg ctg gtg acc gct gcc ctg gtg gcc ttg ggt gtc ctc tac gcc																144
Leu Leu Leu Val Thr Ala Ala Leu Val Ala Leu Gly Val Leu Tyr Ala																
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gac cgc aga ggg atc cca gag gcc caa gag gtg agc gag gtc tgc acc																192
Asp Arg Arg Gly Ile Pro Glu Ala Gln Glu Val Ser Glu Val Cys Thr																
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Thr Pro Gly Cys Val Ile Ala Ala Ala Arg Ile Leu Gln Asn Met Asp																
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Pro Thr Thr Glu Pro Cys Asp Asp Phe Tyr Gln Phe Ala Cys Gly Gly																
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tgg ctg cgg cgc cac gtg atc cct gag acc aac tca aga tac agc atc																336
Trp Leu Arg Arg His Val Ile Pro Glu Thr Asn Ser Arg Tyr Ser Ile																

100						105						110							
ttt	gac	gtc	ctc	cgc	gac	gag	ctg	gag	gtc	atc	ctc	aaa	gcg	gtg	ctg	384			
Phe	Asp	Val	Leu	Arg	Asp	Glu	Leu	Glu	Val	Ile	Leu	Lys	Ala	Val	Leu				
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ctg	tac	cgc	tcc	tgc	atg	aac	cag	agt	gtg	ata	gag	aag	cga	ggc	tct	480			
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Gln	Pro	Leu	Leu	Asp	Ile	Leu	Glu	Val	Val	Gly	Gly	Trp	Pro	Val	Ala				
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atg	gac	agg	tgg	aac	gag	acc	gta	gga	ctc	gag	tgg	gag	ctg	gag	cgg	576			
Met	Asp	Arg	Trp	Asn	Glu	Thr	Val	Gly	Leu	Glu	Trp	Glu	Leu	Glu	Arg				
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cag	ctg	gcg	ctg	atg	aac	tca	cag	ttc	aac	agg	cgc	gtc	ctc	atc	gac	624			
Gln	Leu	Ala	Leu	Met	Asn	Ser	Gln	Phe	Asn	Arg	Arg	Val	Leu	Ile	Asp				
195						200						205							
ctc	ttc	atc	tgg	aac	gac	gac	cag	aac	tcc	agc	cgg	cac	atc	atc	tac	672			
Leu	Phe	Ile	Trp	Asn	Asp	Asp	Gln	Asn	Ser	Ser	Arg	His	Ile	Ile	Tyr				
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Ile	Asp	Gln	Pro	Thr	Leu	Gly	Met	Pro	Ser	Arg	Glu	Tyr	Tyr	Phe	Asn				
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Ser	Val	Ala	Thr	Leu	Leu	Arg	Glu	Asp	Ala	Asn	Leu	Pro	Arg	Asp	Ser				
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Cys	Leu	Val	Gln	Glu	Asp	Met	Met	Gln	Val	Leu	Glu	Leu	Glu	Thr	Gln				
275						280						285							
ctg	gcc	aag	gcc	acg	gta	ccc	cag	gag	gag	aga	cac	gac	gtc	atc	gcc	912			
Leu	Ala	Lys	Ala	Thr	Val	Pro	Gln	Glu	Glu	Arg	His	Asp	Val	Ile	Ala				
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Phe Gly Thr Met Val Glu Glu Val Arg Trp Arg Glu Cys Val Gly Tyr															
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Gln Ile Gly His Pro Asp Tyr Ile Leu Glu Glu Met Asn Arg Arg Leu															
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Val Asn Ala Phe Tyr Ser Pro Asn Arg Asn Gln Ile Val Phe Pro Ala															
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Asn Phe Gly Gly Ile Gly Met Val Ile Gly His Glu Ile Thr His Gly	
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Phe Asp Asp Asn Gly Arg Asn Phe Asp Lys Asn Gly Asn Met Met Asp	
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Trp Trp Ser Asn Phe Ser Thr Gln His Phe Arg Glu Gln Ser Glu Cys	
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Met Ile Tyr Gln Tyr Gly Asn Tyr Ser Trp Asp Leu Ala Asp Glu Gln	
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Phe Phe Ile Asn Tyr Ala Gln Val Trp Cys Gly Ser Tyr Arg Pro Glu	
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Phe Ala Ile Gln Ser Ile Lys Thr Asp Val His Ser Pro Leu Lys Tyr	
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cac tgt gcc cgg ggc acc ccc atg cac ccc aag gag cga tgc cgc gtg	2256
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Leu	Leu	Leu	Val	Thr	Ala	Ala	Leu	Val	Ala	Leu	Gly	Val	Leu	Tyr	Ala	
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Asp	Arg	Arg	Gly	Ile	Pro	Glu	Ala	Gln	Glu	Val	Ser	Glu	Val	Cys	Thr	
	50					55					60					
Thr	Pro	Gly	Cys	Val	Ile	Ala	Ala	Ala	Arg	Ile	Leu	Gln	Asn	Met	Asp	
65					70					75					80	
Pro	Thr	Thr	Glu	Pro	Cys	Asp	Asp	Phe	Tyr	Gln	Phe	Ala	Cys	Gly	Gly	
				85					90					95		
Trp	Leu	Arg	Arg	His	Val	Ile	Pro	Glu	Thr	Asn	Ser	Arg	Tyr	Ser	Ile	
			100					105					110			
Phe	Asp	Val	Leu	Arg	Asp	Glu	Leu	Glu	Val	Ile	Leu	Lys	Ala	Val	Leu	
	115						120					125				
Glu	Asn	Ser	Thr	Ala	Lys	Asp	Arg	Pro	Ala	Val	Glu	Lys	Ala	Arg	Thr	
	130					135					140					
Leu	Tyr	Arg	Ser	Cys	Met	Asn	Gln	Ser	Val	Ile	Glu	Lys	Arg	Gly	Ser	
145				150						155					160	
Gln	Pro	Leu	Leu	Asp	Ile	Leu	Glu	Val	Val	Gly	Gly	Trp	Pro	Val	Ala	
			165					170						175		
Met	Asp	Arg	Trp	Asn	Glu	Thr	Val	Gly	Leu	Glu	Trp	Glu	Leu	Glu	Arg	
		180						185					190			
Gln	Leu	Ala	Leu	Met	Asn	Ser	Gln	Phe	Asn	Arg	Arg	Val	Leu	Ile	Asp	
	195						200					205				
Leu	Phe	Ile	Trp	Asn	Asp	Asp	Gln	Asn	Ser	Ser	Arg	His	Ile	Ile	Tyr	
	210				215						220					
Ile	Asp	Gln	Pro	Thr	Leu	Gly	Met	Pro	Ser	Arg	Glu	Tyr	Tyr	Phe	Asn	
225					230					235					240	
Gly	Gly	Ser	Asn	Arg	Lys	Val	Arg	Glu	Ala	Tyr	Leu	Gln	Phe	Met	Val	
			245						250					255		
Ser	Val	Ala	Thr	Leu	Leu	Arg	Glu	Asp	Ala	Asn	Leu	Pro	Arg	Asp	Ser	
		260						265					270			
Cys	Leu	Val	Gln	Glu	Asp	Met	Met	Gln	Val	Leu	Glu	Leu	Glu	Thr	Gln	
	275					280						285				
Leu	Ala	Lys	Ala	Thr	Val	Pro	Gln	Glu	Glu	Arg	His	Asp	Val	Ile	Ala	

290					295					300					
Leu	Tyr	His	Arg	Met	Gly	Leu	Glu	Glu	Leu	Gln	Ser	Gln	Phe	Gly	Leu
305					310					315					320
Lys	Gly	Phe	Asn	Trp	Thr	Leu	Phe	Ile	Gln	Thr	Val	Leu	Ser	Ser	Val
			325						330					335	
Lys	Ile	Lys	Leu	Leu	Pro	Asp	Glu	Glu	Val	Val	Val	Tyr	Gly	Ile	Pro
			340					345					350		
Tyr	Leu	Gln	Asn	Leu	Glu	Asn	Ile	Ile	Asp	Thr	Tyr	Ser	Ala	Arg	Thr
		355					360					365			
Ile	Gln	Asn	Tyr	Leu	Val	Trp	Arg	Leu	Val	Leu	Asp	Arg	Ile	Gly	Ser
	370					375					380				
Leu	Ser	Gln	Arg	Phe	Lys	Asp	Thr	Arg	Val	Asn	Tyr	Arg	Lys	Ala	Leu
385					390					395					400
Phe	Gly	Thr	Met	Val	Glu	Glu	Val	Arg	Trp	Arg	Glu	Cys	Val	Gly	Tyr
			405						410					415	
Val	Asn	Ser	Asn	Met	Glu	Asn	Ala	Val	Gly	Ser	Leu	Tyr	Val	Arg	Glu
			420					425					430		
Ala	Phe	Pro	Gly	Asp	Ser	Lys	Ser	Met	Val	Arg	Glu	Leu	Ile	Asp	Lys
		435					440					445			
Val	Arg	Thr	Val	Phe	Val	Glu	Thr	Leu	Asp	Glu	Leu	Gly	Trp	Met	Asp
	450					455					460				
Glu	Glu	Ser	Lys	Lys	Lys	Ala	Gln	Glu	Lys	Ala	Met	Ser	Ile	Arg	Glu
465					470					475					480
Gln	Ile	Gly	His	Pro	Asp	Tyr	Ile	Leu	Glu	Glu	Met	Asn	Arg	Arg	Leu
			485					490					495		
Asp	Glu	Glu	Tyr	Ser	Asn	Leu	Asn	Phe	Ser	Glu	Asp	Leu	Tyr	Phe	Glu
			500					505					510		
Asn	Ser	Leu	Gln	Asn	Leu	Lys	Val	Gly	Ala	Gln	Arg	Ser	Leu	Arg	Lys
		515					520					525			
Leu	Arg	Glu	Lys	Val	Asp	Pro	Asn	Leu	Trp	Ile	Ile	Gly	Ala	Ala	Val
	530					535					540				
Val	Asn	Ala	Phe	Tyr	Ser	Pro	Asn	Arg	Asn	Gln	Ile	Val	Phe	Pro	Ala
545					550					555					560
Gly	Ile	Leu	Gln	Pro	Pro	Phe	Phe	Ser	Lys	Glu	Gln	Pro	Gln	Ala	Leu
			565						570					575	
Asn	Phe	Gly	Gly	Ile	Gly	Met	Val	Ile	Gly	His	Glu	Ile	Thr	His	Gly
		580						585					590		
Phe	Asp	Asp	Asn	Gly	Arg	Asn	Phe	Asp	Lys	Asn	Gly	Asn	Met	Met	Asp

595					600					605					
Trp	Trp	Ser	Asn	Phe	Ser	Thr	Gln	His	Phe	Arg	Glu	Gln	Ser	Glu	Cys
610						615					620				
Met	Ile	Tyr	Gln	Tyr	Gly	Asn	Tyr	Ser	Trp	Asp	Leu	Ala	Asp	Glu	Gln
625						630					635				640
Asn	Val	Asn	Gly	Phe	Asn	Thr	Leu	Gly	Glu	Asn	Ile	Ala	Asp	Asn	Gly
				645					650					655	
Gly	Val	Arg	Gln	Ala	Tyr	Lys	Ala	Tyr	Leu	Lys	Trp	Met	Ala	Glu	Gly
			660					665					670		
Gly	Lys	Asp	Gln	Gln	Leu	Pro	Gly	Leu	Asp	Leu	Thr	His	Glu	Gln	Leu
		675					680					685			
Phe	Phe	Ile	Asn	Tyr	Ala	Gln	Val	Trp	Cys	Gly	Ser	Tyr	Arg	Pro	Glu
	690					695					700				
Phe	Ala	Ile	Gln	Ser	Ile	Lys	Thr	Asp	Val	His	Ser	Pro	Leu	Lys	Tyr
705						710					715				720
Arg	Val	Leu	Gly	Ser	Leu	Gln	Asn	Leu	Ala	Ala	Phe	Ala	Asp	Thr	Phe
				725					730					735	
His	Cys	Ala	Arg	Gly	Thr	Pro	Met	His	Pro	Lys	Glu	Arg	Cys	Arg	Val
			740					745					750		
Trp															